

Genital wart

BY

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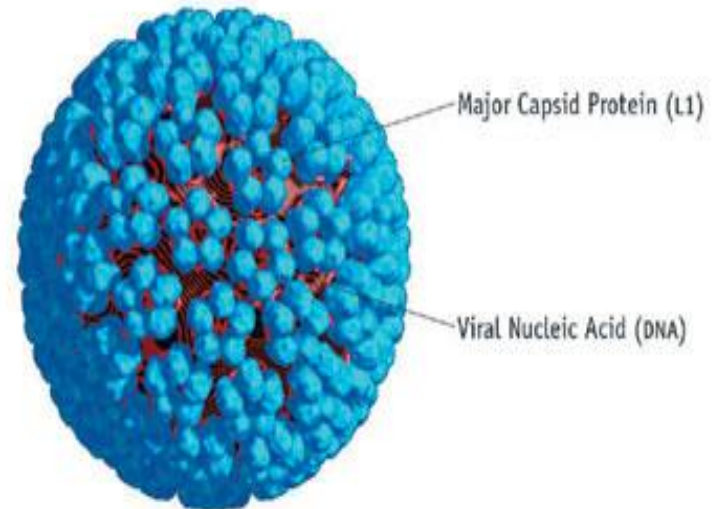
بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

- Genital warts or condylomata acuminata is a sexually transmitted disease caused by the human papilloma virus (HPV).
- condyloma acuminatum, papilloma acuminatum, papilloma venereum, pointed condyloma, pointed wart, venereal wart, verruca acuminata, genital warts

AETIOLOGY

- HPV are are type of papova virus
- HPV are double strand naked DNA viruses
- They replicate inside the nucleus
- Has no envelop (resist drying , freezing and solvents)

THREE-DIMENSIONAL MODEL OF HUMAN PAPILLOMAVIRUS



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Published in The PRN Notebook, Volume 6, Number 3, September 2001 and The PRN Notebook Online at www.prn.org.
Three-dimensional model of HPV created by Louis E. Henderson, Ph.D., Frederick Cancer Research Center.

AETIOLOGY

- High Papilloma viruses are small 50-55 nm diameter DNA viruses that cause squamous epithelial cell proliferation. All papilloma viruses have a tropism for squamous epithelial cells, but different HPV types vary in their specificity for anatomical sites. Anogenital warts are caused by **mucosotropic**

- Approximately 90% of all genital warts are related to HPV types 6 and 11 (HPV-6, HPV-11). These are the least likely to have neoplastic potential .

- More than **100** different types of HPV exist, most of which are harmless. About **30 types** are spread through sexual contact and are classified as either low risk or high risk.
- ***Low risk : 6, 11,*** 34, 40, 42-45, 53-55, 57, 58.
- ***High risk :16, 18,*** 30, 31, 33, 35, 39, 45, 51, 52, 56

Pathophysiology

- HPV invades cells of the basal layer of the epidermis, penetrating skin and mucosal microabrasions in the genital area.
- A **latency period** of months to years.
- viral DNA, capsids, and particles are produced. Host cells become infected and develop genital warts.

INCUBATION PERIOD

- The incubation period of genital wart is long and variable. It is estimated to be around **3 months** with a range from **3 weeks to 8 months**.
- Perinatal acquired HPV infection may not manifest for **up to two years**.

EPIDEMIOLOGY

- *In the US:* Annual incidence is 1%, and genital warts are considered the *most common sexually transmitted disease (STD)*. A 4-fold or more increase in the last 2 decades; prevalence reportedly exceeds 50%.

- *Internationally:* Reports vary on international prevalence, but available data from England, Panama, Italy, the Netherlands, and other developed and underdeveloped countries show HPV infections to be at least as common internationally as in the United States.

- **Sex:** Both sexes are susceptible to infection. Overt disease may be **more common in men** (reported in 75% of cases); however, infection may be more prevalent in women.
- **Age:** Prevalence is greatest in persons aged **17-33 years**, with a peak incidence in persons aged 20-24 years.

TRANSMISSION

Genital warts are *very contagious*.

- *Sexual* : oral, vaginal, or anal sex with an infected partner.
 - About *two-thirds* of people who have sexual contact with a partner with genital warts will develop warts, usually within 3 months of contact.
- *indirect transmission* from *fomites* may occur. Additionally, *passage through vaginal canal at birth* may cause respiratory lesions in infants.

CLINICAL FEATURES

History:

- *Painless blumps, pruritus, and discharge* are the chief complaints with genital warts.
- Generally, two thirds of individuals who have *sexual contact with a partner who has genital warts* develop lesions within 3 months.
- A history involving multiple lesions, rather than a single isolated wart, is more common.
- Involvement of more than 1 area is more common.
- History may indicate previous or other current STDs.

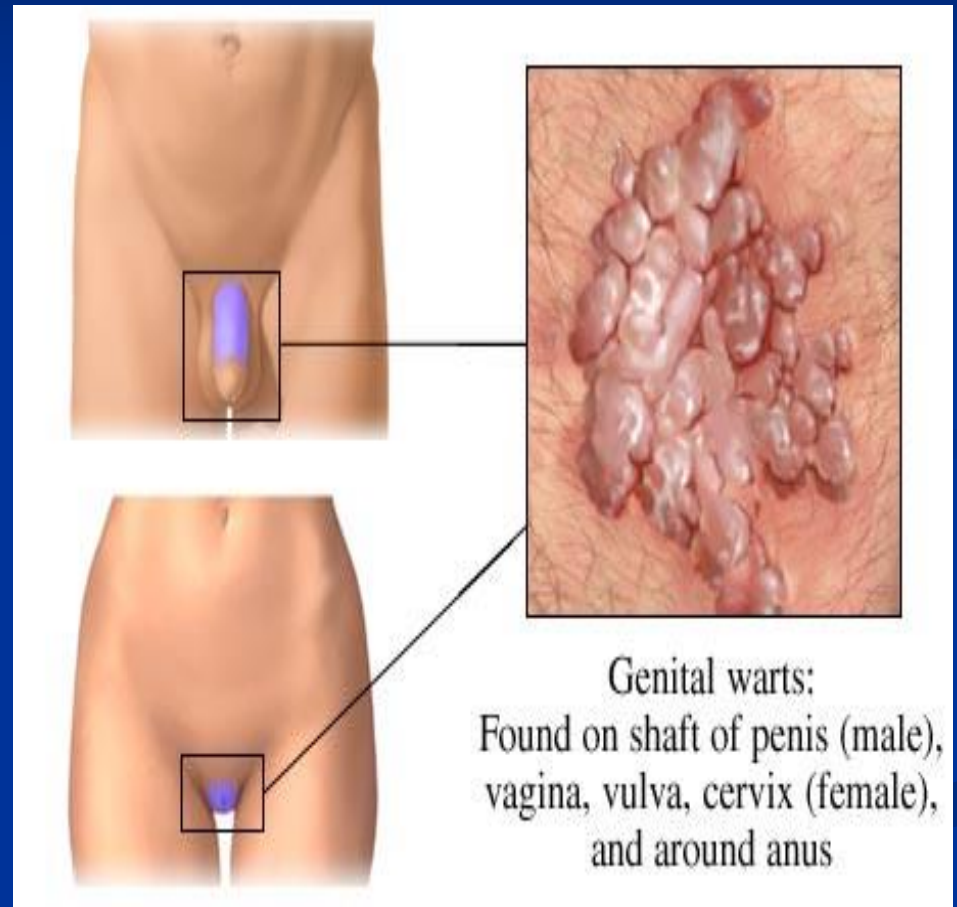
- *Urethral bleeding or urinary obstruction* (uncommon) may be the presenting complaint when the wart involves the meatus.
- *Vaginal bleeding* during pregnancy . Coital bleeding also may occur.
- Latent illness may become active, particularly with pregnancy and immunosuppression.
- Lesions may **regress** spontaneously, remain **static**, or **progress**.

Ex:

- Soft skin colored broad-based, filiform or pedunculated lesions of variable number and size are characteristic of genital warts.
- *On moist area* exuberant rapid growth may occur, forming **cauliflower-like mass** .
- *Over drier areas*, genital warts tend to be more **keratotic** and may look like common wart. At times it may be sufficiently pigmented to resemble seborrheic keratoses. Flat lesions and smooth papular lesions can also be present.
- Growth is enhanced during pregnancy, or in the presence of other local infections.

Site:

- In males warts are most common on the fraenum and coronal sulcus but may be seen anywhere on the genitalia, perianal region, anus and anal canal.
- They are however uncommon on the scrotum. Meatal warts in male may present as bleeding from the urethral orifice.











SFS







warts

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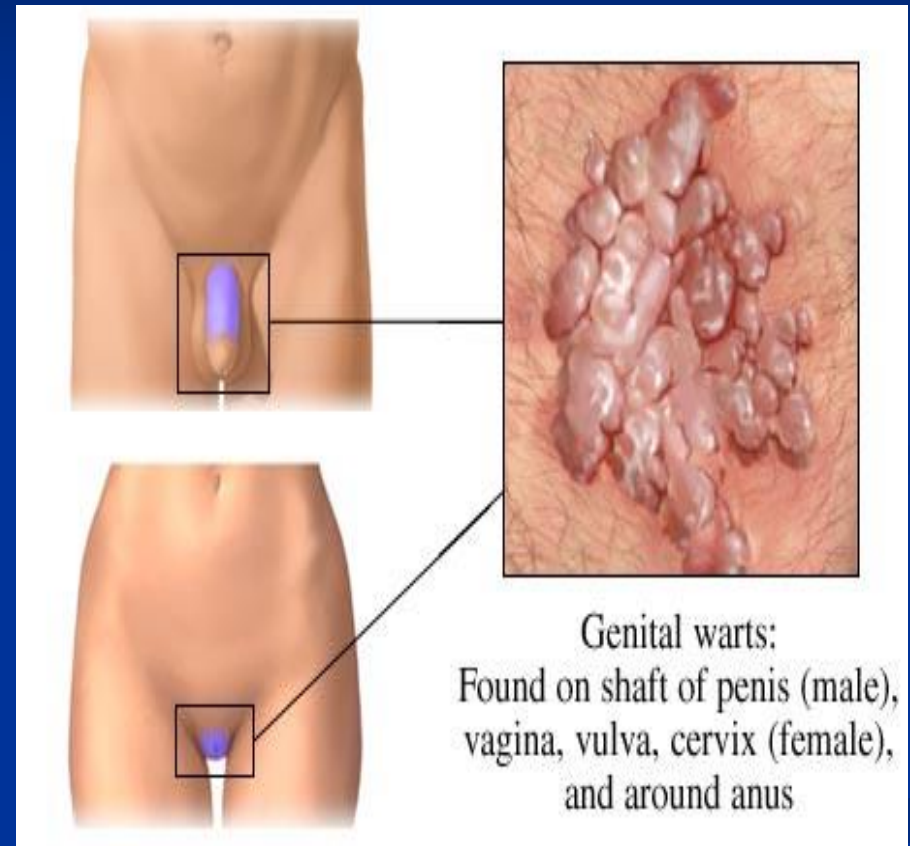




SFS



- In female patients the introitus and labia minora are most commonly affected but any part of the external genitalia and perianal region may be involved also may affect cervix .
- Rarely, genital warts also can develop in mouth or throat if you have oral sex with an infected person.









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COMPLICATIONS

1) *Buschke-Lowenstein Tumor*

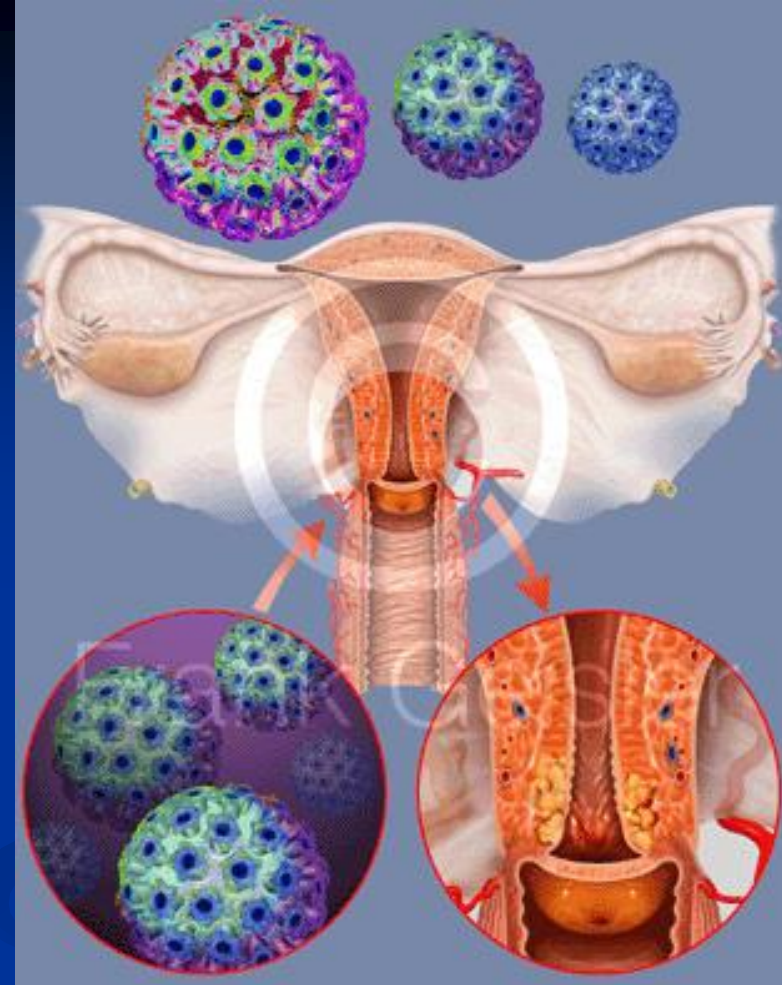
- This lesion enlarged from a pre-existing benign anogenital wart (mainly HPV).
- This is an extremely rare semi-malignant tumor and can occasionally transform into a squamous cell carcinoma.
- There is penetration of underlying tissue by compression that sometimes mimics microinvasion and may create difficulties in differentiating it from a true carcinoma.

2) *Bowenoid Papulosis*

- HPV type 16 has been demonstrated in about 80% of cases.
- It present clinically as *smooth papules that are either erythematous, reddish-violaceous or brownish in colour.*
- Some cases have regressed spontaneously within 1-2 years of observation; in others, the lesions have persisted for more than 10 years.
- Progression to carcinoma or true Bowen's disease is very rare.

3) Cervical Intra-epithelial Neoplasia (CIN) and Invasive Carcinoma

- Epidemiological studies have shown that these condition is associated with HPV infection in particular *type 16 and 18*.



4) Laryngeal Papillomas

- Laryngeal papillomatosis in children is probably acquired from mother with genital warts during delivery. They are usually *type 6 and type 11.*

INVESTIGATION

1) Apply 3-5% acetic acid on suspicious areas and examine these areas after three minutes. This can be used to identify *sub-clinical lesions* which are **whitened**. Both false positive and false negative can occur. The former results from epithelial injury or inflammation.

2) Biopsy done in cases of doubt especially when carcinoma is suspected.

3) *DNA hybridization* for typing of the virus. Although it is mainly of use in research, this tool can now be employed for **medico-legal purpose**.

4) *Pap smear* : Used to look for papillomatosis, acanthosis, koilocytic abnormality, and mild nuclear abnormality

5) *Colposcopy* (stereoscopic microscopy) -

Used to look for papillomatosis, acanthosis, koilocytic abnormality, and mild nuclear abnormality

6) *polymerase chain reaction*

7) *testing for other STDs (eg, HIV, gonorrhea, chlamydia, syphilis).*

Management

General Measures

- Attention to personal hygiene should be emphasized as moistness encourages the growth of warts.
- Circumcision in patients with phimosis may help to clear the warts.
- Use pressure to stop bleeding, if present
- Relieve urethral obstruction .

Specific Therapy

■ Topical:

1. Podophyllin (10-25%)
2. Posalfilin
3. Podophyllotoxin (0.5%)
4. Trichloroacetic acid or Bichloroacetic acid (BCA) 80%–90%.
5. 5-FU (5%)
6. IFN- intralesional
7. imiquimod 5% cream
8. Kunecatechins (Veregen)

■ *Surgery:*

Curettage and cautery

Cryosurgery

CO2 laser

■ *Systemic* : IFN

Podophyllin :

- Podophyllin is a plant-derived resin containing several cytotoxic compounds in unpredictable ratios. The most active of these is **podophyllotoxin**. It may be made up in various concentration (10-25%) with compound benzoin tincture, spirit and liquid paraffin.
- A small amount should be applied to each wart and allowed to air dry. The treatment can be repeated weekly, if necessary.

■ To avoid the possibility of complications associated with systemic absorption and toxicity, two **important guidelines** should be followed:

- 1) application should be limited to **<0.5 mL of podophyllin** or an area of **<10 cm² of warts per session**
- 2) **no open lesions or wounds** should exist in the area to which treatment is administered.
- 3) should be thoroughly **washed off 1–4 hours** after application to reduce local irritation.

Podophyllin is a cytotoxic and anti-mitotic agent and is contraindicated in pregnancy.

Posalfilin :

Posalfilin is a mixture of 20% podophyllin with 10% salicylic acid and is indicated for more **keratotic lesions**. The method of application is similar to podophyllin.

Podophyllotoxin :

- This is one of the active ingredients of podophyllin resin and is available as 0.5% in ethanolic solution (WARTEC). It is an antimitotic agent. It is safer than podophyllin and self-application is allowed in suitable compliant cases.
- The warts should be painted **twice daily for 3 days**, using the applicator provided, and allowed to dry. Treatment may be extended to 4 or 5 days if necessary and tolerated.
- The treatment schedule can be repeated seven days after the first course of treatment if the lesions persist .

Trichloroacetic Acid (TCAA) :

- 30% up to 80%–90% Trichloroacetic acid is used. It is a caustic and should be used with great care and the surrounding skin should be suitably protected. The treated area does not need to be washed after 4 hours as after podophyllin application. *This agent can be used in pregnancy.*
- Both TCA and BCA are caustic agents that destroy warts by *chemical coagulation of proteins.*

Topical 5-fluorouracil (5FU)

- 5-FU cream can be used especially for treatment of urethral and vulvovaginal warts. Local irritation is not uncommon

Imiquimod 5% cream.

- Patients should apply imiquimod cream once daily at bedtime, three times a week for up to 16 weeks.
- The treatment area should be washed with soap and water 6–10 hours after the application. The safety of imiquimod during pregnancy has not been established.
- Genital use: Not recommended for treatment of rectal, cervical, intravaginal, urethral, and intra-anal human papilloma infection; following surgery or drug treatment, do not use topical imiquimod until genital/perianal tissue is healed

Interferons :

- They have been administered **systemically** and **intralesionally** (i.e., injected into the warts).
- intralesional interferon is associated with stinging, burning, and pain at the injection site .
- Interferon is probably effective because of its **antiviral** and/or **immunostimulating** effects.
- **Adult Dose** 250,000 U intralesionally twice weekly for a maximum of 8 wk; not to exceed 2.5 million U / session

Kunecatechins (Veregen)

- Botanical drug product for topical use consisting of extract from **green tea leaves**. Mode of action unknown but does elicit antioxidant activity in vitro. Indicated for topical treatment of **external genital and perianal warts**
- Apply topically tid; use approximately a 0.5-cm strand of ointment topically

Cryosurgery

- Liquid nitrogen is the agent used in our service. It can be applied by using the Cryojet or simply by means of a cotton bud dipped into liquid nitrogen.

Curettage and Cautery

- Curettage and cautery under local anaesthesia may be used for treatment of warts resistant to topical treatment. Scarring is one of the disadvantages of this method.

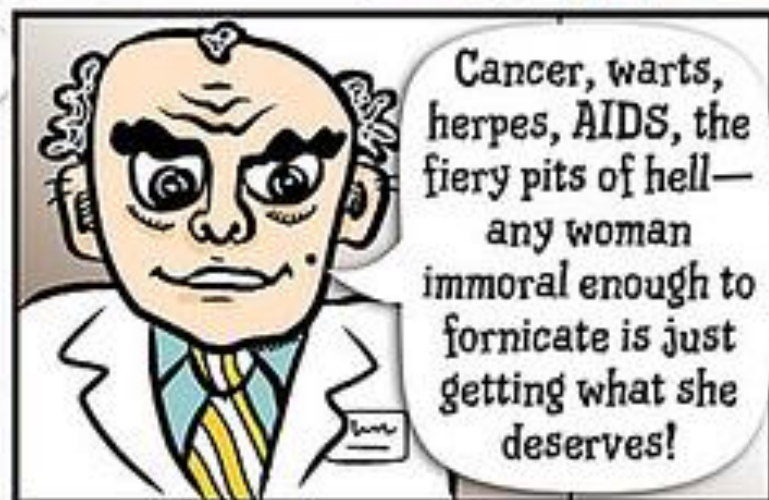
Laser

- The carbon dioxide laser is effective in eradicating some difficult warts. There is recent concern about the infectivity of the carbon dioxide plume generated during the procedure

HPV vaccines

At least 50% of sexually active people will get HPV at some point in their lives, which can lead to cancer in women.

Opponents of the cervical cancer vaccine speak out!



HPV vaccines

- Two HPV vaccine : **Gardasil** and **Cervarix**.

Gardasil : HPV vaccine, was licensed by the Food and Drug Administration (FDA) in June 2006 for the prevention of cervical cancers and other diseases caused by HPV in females.

- It is composed of a viruslike particle consisting of recombinant L1 proteins from HPV types 6, 11, 16, and 18.

- It has been recommended by the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices to be routinely given to girls at age 11-12 years.
- It can be administered starting at age 9 years, with catch-up vaccinations recommended for females aged 13-26 years.

- **Dose** : 0.5 mL IM administered as 3 separate doses; administer second and third doses 2 and 6 mo after first dose
- **Contraindications** Documented hypersensitivity
- **Interactions** Immunosuppressive therapies may decrease immune response to vaccine
- **Pregnancy** B - Usually safe but benefits must outweigh the risks.

■ **Precautions** Shake well before administering; administer in deltoid region of upper arm or in higher anterolateral thigh, do not administer to individuals with bleeding disorders

■ **common adverse** effects include pain, swelling, erythema, and/or pruritus at injection site and fever

Cervarix is HPV vaccine candidate and focuses on cancer prevention with L1 proteins from **HPV types 16 and 18 only**. This vaccine will likely be approved and licensed in late 2006.

Management of Sex Partners

The counseling of sex partners provides an opportunity for these partners to

- 1) learn that HPV infection is common and probably shared between partners
- 2) STD evaluation and screening and Pap screening if they are female.

